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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,502	07/18/2003	Uwe Marx	Weh212T1	3800

7590

09/20/2006

Horst Kasper  
13 Forest Drive  
Warren, NJ 07059

EXAMINER
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AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 09/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/622,502

Applicant(s)

MARX ET AL.

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 11-21 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 22 and 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1-10 and 22 as amended and new claim 24 (6/30/2006) are under examination in the instant office action.

This application contains claims 11-22 and 23 drawn to the invention nonelected with traverse in reply filed 11/28/2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### ***Priority***

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 1/28/2002. It is noted, however, that applicant has not filed a certified copy of the 102 04 382.5 application as required by 35 U.S.C. 119(b).

#### ***Claim Objections***

Claims 5 and 6 as amended are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim 4. See MPEP § 608.01(n).

#### ***Claim Rejections - 35 USC § 112***

Claim 2 as amended is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "mammalian" in the method of claim 1. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-5, 7-10 and 22 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 4,857,464 (Weathers et al) (IDS reference) as explained in the prior office action.

Claims are directed to a method for cultivation animal cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container; step feeding cells with gas/cell cultivation medium mixtures; step obtaining products. Some claims are further drawn to gas/cell cultivation medium mixtures such as mist with droplets up to 5000 micrometers. Some claims are further drawn to feeding by spray generated by ultrasound.

US 4,857,464 (Weathers et al) teaches a method for cultivation cells and obtaining the products from these cells in a mist cultivation reactor wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container with mesh and/or membrane (devices 301 and 302 on Fig. 4 and devices 14 and 33 on Fig. 5) and step of feeding cells with gas/cell cultivation medium mixtures in a form of mist having droplets up to 5000 micrometres (col. 2, lines 45-50) and generated by ultrasound devices (col. 3, lines 1-10). The cells are animal cells including mammalian hydrodomas (table 1; col. 2, line 69; col.5, line 33) that are cultured at high densities or at high yields (col. 5, line 15). The

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products are dissolved in the feeding mixture and collected below the cultivation chambers.

Thus, the cited reference teaches identical steps and structural elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

2. Claims 1-4, 7, 9, 10 and 22 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 6,255,106 (Marx et al) as explained in the prior office action.

Claims are directed to a method for cultivation animal cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the animal cells being mammalian cells. Some claims are further drawn to the use of semipermeable membrane for separation. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid.

US 6,255,106 (Marx et al) teaches a method for cultivation mammalian cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures and step obtaining product (Fig. 1; col. 1, lines 56-65; col. 2, lines 28-30 and lines 52). Thus, the cited reference teaches identical steps and structural elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

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3. Claims 1-7, 9, 10, 22 and amended and new claim 24 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by Knazek (Federation Proceedings. 1974. Vol.33, NO. 8, pages 1978-1981) as explained in the prior office action.

Claims are directed to a method for cultivation animal cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the cells being mammalian cells. Some claims are further drawn to the use of semipermeable membrane for separation and to membrane made from polycarbonate. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid.

The reference by Knazek discloses a method for cultivation mammalian cells at high densities for obtaining the secretion products from these cells wherein the method comprises step of culturing cells on polycarbonate capillaries or in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures (fig. 2) and step obtaining secretion products, for example: prolactin (see fig. 2). Thus, the cited reference teaches identical steps and structural elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-10 and 22 as amended and new claim 24 remain/are rejected under 35 U.S.C.

103(a) as being unpatentable over US 4,857,464 (Weathers et al), US 6,255,106 (Marx et al) and Knazek (Federation Proceedings. 1974. Vol.33, NO. 8, pages 1978-1981) as explained in the prior office action.

Claims are directed to a method for cultivation animal cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the cells being plant or mammalian cells. Some claims are further drawn to the use of semipermeable membrane for separation and to membrane made from polycarbonate. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid or in a form of mist having droplets up to 5000 micrometres. Some claims are further drawn to feeding by spray generated by ultrasound.

The cited US 4,857,464 (Weathers et al), US 6,255,106 (Marx et al) and Knazek are relied upon as explained above for the disclosure of culturing cells including plant cells and mammalian cells at high densities for obtaining the products from these cells. The semipermeable membranes used for separation of cultivation chambers from supply container in all cited methods and the membrane materials include polycarbonate (Knazek). The feeding of cells is provided by gas/cell cultivation medium mixtures in all cited methods including the use of mist having droplets up to 5000 micrometres (US 4,857,464).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify membrane materials and form of gas/liquid feeding mixtures with a reasonable expectation of success in culturing cells including plant cells and mammalian cells at high densities for obtaining the products from these cells as adequately demonstrated by the cited references. It would be within the purview of ordinary skill in the art to adjust form of gas/liquid feeding mixtures with regard to the cells used for production of desired products and to choose membrane materials that are available and known for culturing cells.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

### ***Response to Arguments***

Applicant's arguments filed 6/30/2006 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 4,857,464 (Weathers et al) applicants appear to argue (response pages 14-15) that the cited method does not provide for culturing cells at high density due to a large surface of cultivation grid that would require immobilization and that would not allow for high density of cells. Yet, the claimed invention neither defines any relationship between cell density and surfaces of the cell cultivation chambers nor it is explicitly drawn to culturing cells in suspensions. Moreover,



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the cited method provides for cultivation of both non-attaching and attaching animal cells, for example: see col. 5, line 32. Applicants also argue that "high yields" in col. 5, line 15 of the cited reference does not mean "high density" as claimed. However, given broadest meaning of the claimed term "high" cell density, it is reasonable to assume that high yield of useful products as disclosed by the cited patent is a result of high cell density.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 6,255,106 (Marx et al) applicants appear to argue (response page 16) that the cited method does not provide for "high" cell density due to insufficient oxygen supply. Yet, the claimed method recites feeding animal cells with a generic "gas/cell cultivation medium mixture". Moreover, the cited patent teaches that "by means of oxygenator, the medium is supplied with oxygen", for example see col. 2, lines 21-22. Thus, the cited method as disclosed is not considered to be different from the method as claimed.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by Knazek applicants appear to admit that the reference in fact describes cultivation of cells at high cell densities (response page 17). Applicants further argue that the oxygen supply in the cited method is questionable. However, the cited reference teaches incorporation of the same materials as required by the claimed invention (claims 6 and 24, for example) such as polycarbonate materials in order "to increase oxygen diffusion" (see the Knazek's reference at page 1979, col. 2, lines 18-22).

With regard to the claim rejection under 35 USC § 103 applicants argue that the cited prior art does not resolve problem of oxygen supply of animal cells in a sufficient manner.

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This argument is not found particularly persuasive because the cited references are in the same field of endeavor such as cultivation of animal cells for obtaining products and they seek to solve the same problems as the instant application and claims including means for providing animal cells with gas/liquid nutrient mixture in order to increase final yields of beneficial products, and one of skill in the art is free to select components available in the prior art, *In re Winslow*, 151 USPQ 48 (CCPA, 1966).

No claims are allowed.

#### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

September 15, 20065

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER